

AMENDMENTS TO THE CLAIMS

Claim 1. (Currently amended):

A transgenic animal mouse whose genome contains a a homozygous disruption of both the endogenous *Gpx1* gene and *Gpx2* genes wherein said animal mouse develops cancer.

Claim 2. (Currently amended):

A cell from the transgenic animal mouse of claim 1.

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Claims 3-4. (Canceled).

Claim5. (Currently amended):

A cell of claim 4 2 which is selected from the group consisting of stem cells, epithelial cells and myelofibroblasts.

Claim 6. (Currently amended):

The transgenic mouse of claim 3 1 wherein the genetic background of the mouse is selected from the group consisting of a B6 mouse, a 129Sv/J hybrid mouse, a 129S3 hybrid mouse and a $\frac{1}{2}$ B6, 1/4 129Sv/J and 1/4 129S3 hybrid mouse.

Claim 7. (Currently amended):

A transgenic mouse as in claim 3 1 which further comprises a mouse which is a germ free mouse.

Claim 8. (Currently amended):

A transgenic ~~animal~~ mouse as in claim 3 1 wherein the cancer is selected from the group consisting of ileal cancer and myeloleukemia.

Claim 9. (Currently amended):

An animal model for cancer which comprises a transgenic ~~animal~~ mouse whose genome comprises a homozygous disruption of the endogenous *Gpx1* gene and a homozygous disruption of the endogenous *Gpx2* gene and wherein disruption of the *Gpx1* and *Gpx2* genes is sufficient to effect one or more signs or symptoms in the ~~animal~~ mouse associated with cancer.

and

Claim 10. (Canceled).

Claim 11. (Currently amended):

The model of claim ~~10~~ 9 wherein the cancer is ileal cancer.

Claim 12. (Original):

The model of claim 11 wherein the sign or symptom associated with cancer is selected from the group consisting of ileitis, colitis, hypothermia, decreased rate of weight gain, perianal ulceration, diarrhea, wasting syndrome, inflammatory bowel disease, dysplasia in the small bowel, one or more tumors in the small bowel.

Claim 13. (Currently amended):

The model of claim ~~10~~ 9 wherein the cancer is myeloleukemia.

Claim 14. (Currently amended):

The model of claim ~~10~~ 9 wherein the genetic background of the mouse is selected from the group consisting of a B6 mouse, a 129Sv/J hybrid mouse, a 129S3 hybrid mouse and a 1/2 B6, 1/4 129Sv/J and 1/4 129S3 hybrid mouse.

Claim 15. (Currently amended):

A model as in claim ~~10~~ 9 wherein the mouse further comprises a mouse which is a germ free mouse.

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Int*
Claim 16. (Currently amended):

A method to screen for potential therapeutic agents for the treatment of cancer which comprises the steps of:

- a) administering a potential therapeutic agent to a first transgenic animal mouse whose genome comprises a homozygous disruption of both the endogenous *Gpx1* gene and *Gpx2* genes and
- b) maintaining the animal mouse for a time sufficient to permit the detection of a change in one or more signs or symptoms in the animal mouse associated with cancer in the transgenic animal mouse;
- c) observing the animal mouse for a change in at least one sign or symptom associated with cancer, wherein a second transgenic animal mouse having the same genetic background as the first transgenic animal mouse and whose genome also comprises a homozygous disruption of both the endogenous *Gpx1* gene and *Gpx2* genes has been maintained under the same conditions as the first animal mouse but has not received the potential therapeutic agent; and

Original

d) determining whether one or more signs or symptoms associated with cancer is present in the second transgenic animal mouse but not in the first transgenic animal mouse;
wherein a potential therapeutic agent will be one that causes a lower incidence of at least one sign or symptom associated with cancer in the first transgenic animal mouse.

Claim 17. (Canceled).

Claim 18. (Currently amended):

A method as in claim ~~17~~ 16 wherein the cancer is ileal cancer.

Claim 19. (Currently amended):

The ~~model~~ method of claim 18 wherein the sign or symptom associated with cancer is selected from the group consisting of ileitis, colitis, hypothermia, decreased rate of weight gain, perinatal ulceration, diarrhea, wasting syndrome, inflammatory bowel disease, dysplasia in the small bowel, one or more tumors in the small bowel.

Claim 20. (Currently amended):

The method of claim ~~17~~ 16 wherein the cancer is myeloleukemia

Claim 21. (Currently amended):

A method as in claim ~~17~~ 16 wherein the genetic background of the mouse is selected from the group consisting of a B6 mouse, a 129Sv/J hybrid mouse, a 129S3 hybrid mouse and a ½ B6, 1/4 129Sv/J and 1/4 129S3 hybrid mouse.

Claim 22. (Currently amended):

A method as in claim ~~17~~ 16 wherein the mouse further comprises a mouse which is a germ free mouse.

Claim 23. (Currently amended):

A method as in claim ~~17~~ 16 wherein determination of whether one or more signs or symptoms associated with cancer is present in the second mouse but not in the first mouse comprises sacrificing the first and second mouse after a time sufficient for the detection of at least one sign or symptom associated with cancer in the first mouse and second mouse has elapsed.

Amended

Claim 24. (Currently amended):

The method as in claim ~~17~~ 16 wherein the determination of whether one or more signs or symptoms associated with cancer is present in the second mouse but not in the first mouse comprises withdrawing a body fluid or other bodily substance from the first and second mouse and analyzing the body fluid for the presence of one or more signs or symptoms associated with cancer is present.

Claim 25. (Original):

The method as in claim 24 wherein the bodily fluid is selected from the group consisting of blood and stool.

Claims 26-39. (Canceled).

Claim 40. (Original):

A transgenic double knockout mouse whose genome comprises a homozygous disruption of the endogenous *Gpx1* gene and a homozygous disruption of the endogenous *Gpx2* gene, wherein each disruption comprises the insertion of a transgene, and wherein the combined disruptions result in a decreased level of GPX-1 and GPX-GI production and decreased number of cells producing GPX-I and GPX-GI in the transgenic mouse as compared to a nontransgenic mouse.

Claim 41. (Original):

A transgenic double knockout mouse as in claim 40 which exhibits one or more physiological symptoms selected from the group consisting of ileitis, colitis, hypothermia, decreased rate of weight gain, perianal ulceration, diarrhea, wasting syndrome, inflammatory bowel disease and cancer of the lower gastro-intestinal tract.

Claim 42. (Original):

A cell isolated from a double knockout mouse as in claim 40.

Claim 43. (Original):

A cell as in claim 42, selected from the group consisting of a stem cell, an epithelial cell and a myofibroblast.

Claim 44. (Original):

A cell as in claim 43 which is a stem cell.

Claim 45. (Original):

A cell as in claim 43 which is an epithelial cell.

Claim 46. (Original):

A cell as in claim 43 which is a myofibroblast.

Claim 47. (Original):

A transgenic double knockout mouse as in claim 40 which further comprises a mouse which is a germ free mouse.

Claim 48. (Original):

A transgenic double knockout mouse as in claim 1 wherein said knockout mouse is a mouse with a B6 genetic background.

Claim 49. (Original):

A transgenic double knockout mouse as in claim 1 wherein said knockout mouse is a mouse with a hybrid mouse having a $\frac{1}{2}$ B6, $\frac{1}{4}$ 129 SuJ and $\frac{1}{4}$ 129 S3 genetic background.

Claims 50-59. (Canceled).

Claim 60. (Original):

A transgenic mouse which has a homozygous knockout of the *Gpx1* gene and a heterozygous knockout of one allele of the *Gpx2* gene.

Claim 61. (Original):

An animal model for the study of the degree of functional redundancy of GPX-1 and GPX-GI in the ileum and colon comprising the mouse of claim 60.

Claim 62. (Original):

A transgenic mouse which has a homozygous knockout of the *Gpx2* gene and a heterozygous knockout of one allele of the *Gpx1* gene.


Claim 63. (Original):

An animal model for the study of the degree of functional redundancy of GPX-1 and GPX-GI in the ileum and colon comprising the mouse of claim 62.

Claims 64-66. (Canceled).
